PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

To:

BRANTS, Johan, Philippe, Emile
De Clercq, Brants & Partners
E. Gevaertdreef 10a
B-9830 Sint-Martens-Latem
BELGIQUE

Date of mailing *(day/month/year)*	23.11.2004
Applicant's or agent's file reference	**IMPORTANT NOTIFICATION**
UNI-001-PCT	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/11194	09.10.2003	09.10.2002

Applicant
UNIBIOSCREEN S.A. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hebert, W Tel. +49 89 2399-2152

Form PCT/IPEA/416 (...)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UNI-001-PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/11194	International filing date *(day/month/year)* 09.10.2003	Priority date *(day/month/year)* 09.10.2002
International Patent Classification (IPC) or both national classification and IPC C07D513/20		
Applicant UNIBIOSCREEN S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 19 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
05.05.2004	23.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Boletti-Cremers, K Telephone No. +49 89 2399-8541

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/11194

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1, 3-26, 30-73	as originally filed
27, 28	filed with telefax on 30.08.2004
2, 2a, 29, 29a	received on 03.11.2004 with letter of 03.11.2004

Claims, Numbers

1-32	received on 03.11.2004 with letter of 03.11.2004

Drawings, Sheets

1/13-13/13	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 32

   because:

   ☒ the said international application, or the said claims Nos. 32 relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-32
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-32
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-31
	No:	Claims	

2. Citations and explanations

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/11194

see separate sheet

POINT III.

For the assessment of the presently worded claim 32, on the question whether it is industrially applicable, no unified criteria exist in the PCT.
The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognise as industrially applicable claims to the use of a compound in medical treatment, but will allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a new medical treatment.

POINT V.

The following documents , quoted in the I.S.R., have been considered as relevant for the examination of the present application . Their numbering will be adhered to for the rest of the procedure.

D1: WO-A-98 52562, cited in the application.
D2: J.A.C.S, organic and bio-organic chemistry, 1983, 12, pp. 2827-35.
D3: US-A-5 645 988.

1. Novelty.

1.1 In view of the fact that the compounds of present invention as claimed are not disclosed in D1 because they possess a saturated spiro-condensed thioazolidine ring instead of the insaturated version of uscharin and that possibly said ring must be substituted , they can be regarded as novel with respect to the content of D1.
Moreover, some of the presently claimed compounds differ merely from the uscharin of D1 in that they are merely characterised by the defined substituents R_1 as on file and , therefore, they can also be regarded as novel with respect to the content of D1.

1.2 Insofar as compounds (1b), (3c) and (3b) of D2 are not part of claimed matter because they are either non substituted derivatives of those (substituted) of the claims, or they

are substituted differently on position 19 (cf. R^1 is different).
Consequently , the claimed matter can be regarded as novel with respect to the content of D2.

1.3 In view of the fact that the compound named 650362 of D3 does not fall within the scope of the claims on file , they can be regarded as novel with respect to its content.

2. Inventiveness.

In view of the comparative data which are encompassed in the description and which show the advantages of the claimed compounds in comparison with uscharin, the inventiveness towards D1 and D2 can be acknowledged.

3. Formal Objection.

The attention of the Applicant is already drawn to the fact that he will be faced with an objection towards the content of present claim 23 when the application will reach the European regional proceedings because said claim refers to the description which is not allowable (see Rule 29 (6) EPC) according to the EPC.

Compositions comprising uscharin or salts thereof have been reported to be usable for treatment of medical conditions related to cell proliferation. For example, US patent No 6,342,490 and WO- 9852562 both describe compositions comprising uscharin or salts thereof and the use of uscharin to combat cell proliferation, e.g. in the treatment of cancer.

Some of the known cardenolide glycosides, f.e. calotropin and uzarigenin, are cytotoxic for cell cultures but are not mentioned to show *in vivo* tumor-inhibiting activity. Also uscharin has been shown to have some cytotoxic activity on tumor cells *in vitro*. In addition, uscharin was also described to have *in vivo* tumor-inhibiting effects, as for instance described in US patent No 6,342,490. Derivatives of uscharin have not been reported so far to be useful for medical applications.

Cheung et al. (1983; J. Chem. Soc. Perkin Transactions 1: Organic and bio-organic chemistry (1971-1999) (12) 2827-235) disclose the stereochemistry of cardenolide glycosides of Asclepiadaceae including 19-deoxyuscharin, uscharin and voruscharin.

In US 5,645,988 methods of identifying drugs with selective effects against cancer cells are presented. The drug indicated with 650362 shows some similarity with uscharin.

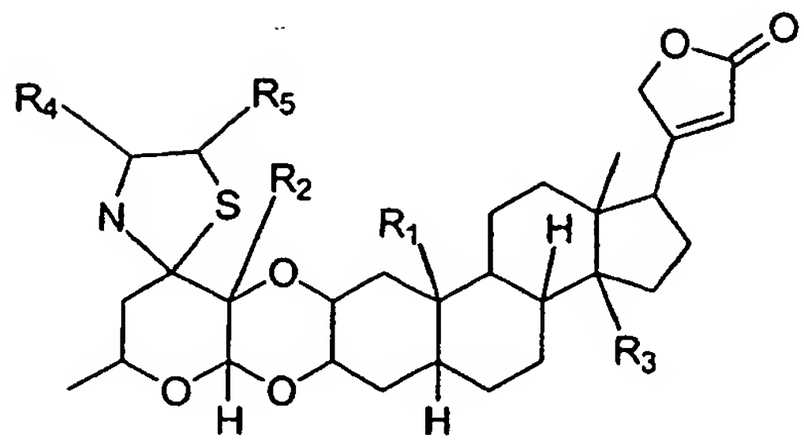
It is a general object of the present invention to provide novel cardenolide glycosides, which have a cytotoxic activity. It is another general object of the present invention to provide novel cardenolide glycosides, which can be exploited in medical applications.

SUMMARY

In a first aspect, the present invention relates to a compound of the formula I or a pharmaceutically acceptable salt thereof,

2a

formula I



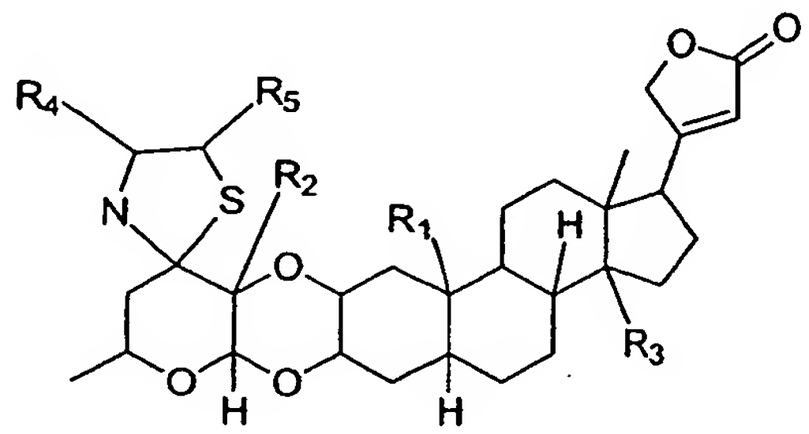
wherein R^1 is selected from the group comprising hydrogen, alkyl, alkenyl, alkynyl, alkyloxy, alkyloxyalkyl, alkylthioalkyl, alkyloxycarbonyl, alkylthiocarbonyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylthiocarbonyl, cycloalkylalkoxycarbonyl, cycloalkylalkoxythiocarbonyl, cycloalkylthioalkyl,

from the group indicated in above; wherein R^2 and R^3 are hydroxyl and wherein R^4 and R^5 are hydrogen or alkyl.

In another preferred embodiment, the invention relates to an uscharin derivative having the formula Ia, wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, cycloalkylalkyl, silyloxyalkyl, aralkyl, arylalkenyl, carboxyl, Het^{1}oxyalkyl, Het^{1}aryloxyalkyl, Het^{1}alkyloxyalkyl, Het^{2}oxyalkyl, Het^{2}alkyloxyalkyl, Het^{2}aryloxyalkyl, optionally substituted by one or more substituents independently selected from the group indicated above; wherein R^2 and R^3 are hydroxyl and wherein R^4 and R^5 are hydrogen.

Another further embodiment of the invention relates to a compound of formula Ib,

formula Ib



wherein R^1 is selected from the group comprising alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, alkyloxycarbonyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylalkoxycarbonyl, cycloalkylthioalkyl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, cycloalkylcarbonyloxyalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, aryloxycarbonyl, aralkoxycarbonyl, arylthioalkyl, aralkanoyl, aroyl, silyloxyalkyl, carboxyl, alkenylcarbonyl, alkynylcarbonyl, Het^{1}oxyalkyl, Het^{1}alkoxycarbonyl, Het^{1}oxycarbonyl, Het^{1}aryloxyalkyl, Het^{1}alkyloxyalkyl, Het^{1}arylthioalkyl, Het^{1}aryloxycarbonyl, Het^{1}aralkoxycarbonyl, Het^{1}oxyalkylcarbonyl, Het^{1}alkyloxyalkylcarbonyl, Het^{1}aryloxyalkylcarbonyl, Het^{1}carbonyloxyalkyl, Het^{1}alkylcarbonyloxyalkyl, Het^{1}aralkylcarbonyloxyalkyl, Het^{2}oxyalkyl, Het^{2}alkyloxyalkyl, Het^{2}oxycarbonyl, Het^{2}alkoxycarbonyl, Het^{2}aralkoxycarbonyl, Het^{2}aryloxycarbonyl, Het^{2}aryloxyalkyl, Het^{2}arylthioalkyl, Het^{2}oxyalkylcarbonyl, Het^{2}alkyloxyalkylcarbonyl, Het^{2}aryloxyalkylcarbonyl, Het^{2}carbonyloxyalkyl, Het^{2}alkylcarbonyloxyalkyl, Het^{2}aralkylcarbonyloxyalkyl, $CR^6{=}NR^7$, $CR^6{=}N(OR^7)$,

with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^1 is optionally substituted by one or more substituents independently selected from the group as indicated above,

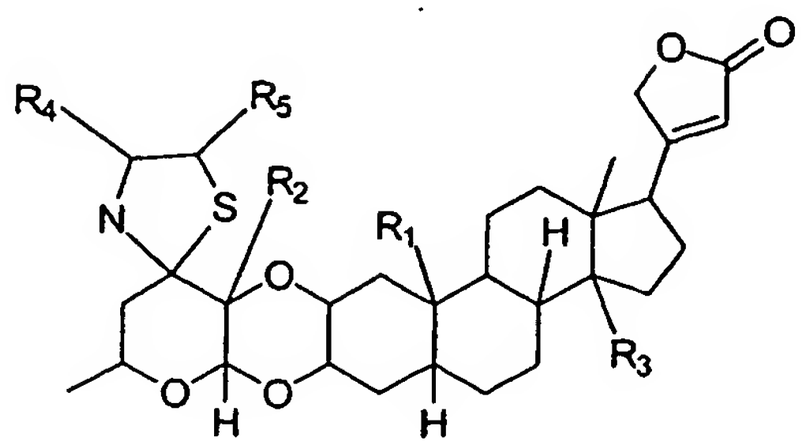
wherein R^2 and R^3 are hydroxyl and wherein R^4 is replaced by a double bond between the N atom and the C carbon atom of the N-containing heterocyclic ring of formula I; and wherein R^5 is hydrogen.

According to this embodiment, this compound may also be represented by the formula III:

CLAIMS

1. A compound of the formula I or a pharmaceutically acceptable salt thereof,

formula I



wherein R^1 is selected from the group comprising hydrogen, alkyl, alkenyl, alkynyl, alkyloxy, alkyloxyalkyl, alkylthioalkyl, alkyloxycarbonyl, alkylthiocarbonyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylthiocarbonyl, cycloalkylalkoxycarbonyl, cycloalkylalkoxythiocarbonyl, cycloalkylthioalkyl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, cycloalkylcarbonyloxyalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, aryloxycarbonyl, arylthiocarbonyl, aralkoxycarbonyl, arylalkylthiocarbonyl, aryloxyalkyl, arylthioalkyl, haloalkyl, hydroxyalkyl, aralkanoyl, aroyl, aryloxycarbonylalkyl, aryloxyalkanoyl, carboxyl, formyl, alkenylcarbonyl, alkynylcarbonyl, Het^1, Het^1alkyl, Het^1oxyalkyl, Het^1aryl, Het^1aralkyl, Het^1cycloalkyl, Het^1carbonyl, Het^1alkoxycarbonyl, Het^1alkylthiocarbonyl, Het^1oxycarbonyl, Het^1thiocarbonyl, Het^1alkanoyl, Het^1aralkanoyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^1aryloxycarbonyl, Het^1aralkoxycarbonyl, Het^1aroyl, Het^1oxyalkylcarbonyl, Het^1alkyloxyalkylcarbonyl, Het^1aryloxyalkylcarbonyl, Het^1carbonyloxyalkyl, Het^1alkylcarbonyloxyalkyl, Het^1aralkylcarbonyloxyalkyl, Het^2alkyl; Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aralkyl, Het^2carbonyl, Het^2oxycarbonyl, Het^2thiocarbonyl, Het^2alkanoyl, Het^2alkylthiocarbonyl, Het^2alkoxycarbonyl, Het^2aralkanoyl, Het^2aralkoxycarbonyl, Het^2aryloxycarbonyl, Het^2aroyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, Het^2oxyalkylcarbonyl, Het^2alkyloxyalkylcarbonyl, Het^2aryloxyalkylcarbonyl, Het^2carbonyloxyalkyl, Het^2alkylcarbonyloxyalkyl, Het^2aralkylcarbonyloxyalkyl, cyano, aminocarbonyl, aminoalkanoyl, aminoalkyl, $CR^6=NR^7$ or $CR^6=N(OR^7)$, with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^2 and R^3 are independently selected from the group comprising hydroxyl, alkyloxy, alkylsilyloxy, arylsilyloxy, alkyloxyalkyloxy, cycloalkyloxy cycloalkylalkyloxy, aralkyloxy, aryloxyalkyloxy, silyloxy, alkylcarbonyloxy, arylcarbonyloxy, cycloalkylcarbonyloxy, haloalkyloxy, hydroxyalkyloxy, aralkanoyloxy, aroyloxy, aryloxycarbonylalkyloxy, formyloxy, Het^1alkyloxy, Het^1oxy, Het^1oxyalkyloxy, Het^1aryloxy, Het^1aralkyloxy, Het^1cycloalkyloxy, Het^1carbonyloxy, Het^1oxycarbonyloxy, Het^1alkanoyloxy, Het^1aralkanoyloxy, Het^1aryloxyalkyloxy, Het^1aroyl, Het^2oxy, Het^2alkyloxy; Het^2oxyalkyloxy, Het^2aralkyloxy, Het^2cycloalkyloxy, Het^2alkanoyloxy, Het^2aralkanoyloxy, Het^2carbonyloxyl, Het^2aryloxy, Het^2aryloxyalkyloxy,

wherein R^1 R^2 and R^3 are optionally substituted by one or more substituents independently selected from the group comprising alkyl, aralkyl, aryl, Het^1, Het^2, cycloalkyl, alkyloxycarbonyl, carboxyl, aminocarbonyl, mono- or di(alkyl)aminocarbonyl, aminosulfonyl, alkyl$S(=O)_t$, hydroxy, cyano, halogen or amino optionally mono- or disubstituted wherein the substituents are independently selected from the group comprising alkyl, aryl, aralkyl, aryloxy, arylamino, arylthio, aryloxyalkyl, arylaminoalkyl, aralkoxy, alkylthio, alkoxy, aryloxyalkoxy, arylaminoalkoxy, aralkylamino, aryloxyalkylamino, arylaminoalkylamino, arylthioalkoxy, arylthioalkylamino, aralkylthio, aryloxyalkylthio, arylaminoalkylthio, arylthioalkylthio, alkylamino, cycloalkyl, cycloalkylalkyl, Het^1, Het^2, Het^1alkyl, Het^2alkyl, Het^1amino, Het^2amino, Het^1alkylamino, Het^2alkylamino, Het^1thio, Het^2thio, Het^1alkylthio, Het^2alkylthio, Het^1oxy and Het^2oxy, OR^8, SR^8, $SO_2NR^8R^9$, $SO_2N(OH)R^8$, CN, $CR^8{=}NR^9$, $S(O)R^8$, SO_2R^8, $CR^8{=}N(OR^9)$, N_3, NO_2, NR^8R^9, $N(OH)R^8$, $C(O)R^8$, $C(S)R^8$, CO_2R^8, $C(O)SR^8$, $C(O)NR^8R^9$, $C(S)NR^8R^9$, $C(O)N(OH)R^9$, $C(S)N(OH)R^8$, $NR^8C(O)R^9$, $NR^8C(S)R^9$, $N(OH)C(O)R^9$, $N(OH)C(S)R^8$, $NR^8CO_2R^9$, $NR^8C(O)NR^9R^{10}$, and $NR^8C(S)NR^9R^{10}$, $N(OH)CO_2R^8$, $NR^8C(O)SR^9$, $N(OH)C(O)NR^8R^9$, $N(OH)C(S)NR^8R^9$, $NR^8C(O)N(OH)R^9$, $NR^8C(S)N(OH)R^9$, $NR^8SO_2R^9$, $NHSO_2NR^8R^9$, $NR^8SO_2NHR^9$, $P(O)(OR^8)(OR^9)$,

with t being an integer between 1 and 2, and R^8 R^9 and R^{10} being each independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^4 is selected from the group comprising oxo, hydroxyl, alkyl, alkenyl, alkynyl, alkanediyl, alkyloxy, alklylthio, alkylamino, alkyloxyalkyl, arylcarbonylalkyl, alkylcarbonylalkyl, alkanoyl, cycloalkylcarbonylalkyl,

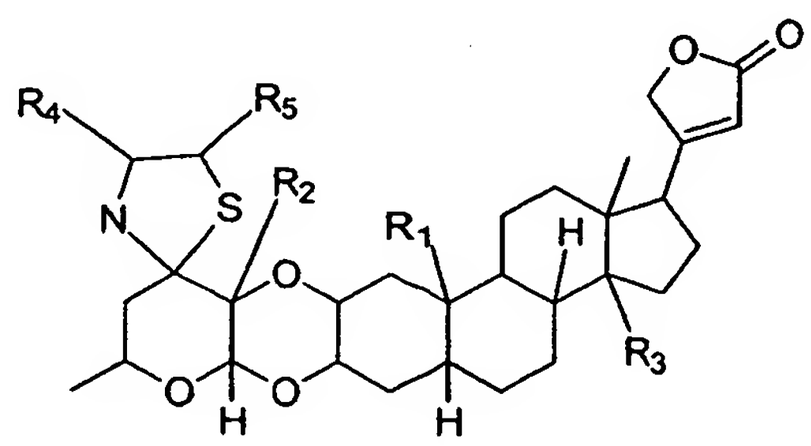
cycloalkyl, cycloalkyloxy, cycloalkylthio, cycloalkylamino, cycloalkylalkyl, cycloalkylalkanoyl, aryl, aralkyl, arylalkenyl, arylcarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aryloxyalkyl, haloalkyloxy, haloalkylthio, haloalkylamino , hydroxyalkyl, aralkanoyl, aryloxycarbonylalkyl, aryloxyalkanoyl, Het^1, Het^1alkyl, Het^1oxy, Het^1oxyalkyl, Het^1aryl, Het^1aralkyl, Het^1cycloalkyl, Het^1aryloxyalkyl, Het^1aroyl, Het^2, Het^2oxy, Het^2alkyl; Het^2oxyalkyl, Het^2aralkyl, Het^2cycloalkyl, Het^2aryl, Het^2alkanoyl, Het^2aralkanoyl, Het^2aroyl, Het^2aryloxyalkyl, aminocarbonyl, aminoalkanoyl, aminoalkyl, optionally substituted by one or more substituents independently selected from the group comprising alkyl, aralkyl, aryl, Het^1, Het^2, cycloalkyl, alkyloxycarbonyl, carboxyl, aminocarbonyl, mono- or di(alkyl)aminocarbonyl, aminosulfonyl, $alkylS(=O)_t$, hydroxy, cyano, halogen or amino optionally mono- or disubstituted wherein the substituents are independently selected from the group comprising alkyl, aryl, aralkyl, aryloxy, arylamino, arylthio, aryloxyalkyl, arylaminoalkyl, aralkoxy, alkylthio, alkoxy, aryloxyalkoxy, aylaminoalkoxy, aralkylamino, aryloxyalkylamino, arylaminoalkylamino, arylthioalkoxy, arylthioalkylamino, aralkylthio, aryloxyalkylthio, arylaminoalkylthio, arylthioalkylthio, alkylamino, cycloalkyl, cycloalkylalkyl, Het^1, Het^2, Het^1alkyl, Het^2alkyl, Het^1amino, Het^2amino, Het^1alkylamino, Het^2alkylamino, Het^1thio, Het^2thio, Het^1alkylthio, Het^2alkylthio, Het^1oxy and Het^2oxy, OR^{11}, SR^{11}, $SO_2NR^{11}R^{12}$, $SO_2N(OH)R^{11}$, CN, $CR^{11}=NR^{12}$, $S(O)R^{11}$, SO_2R^{11}, $CR^{11}=N(OR^{12})$, N_3, NO_2, $NR^{11}R^{12}$, $N(OH)R^{11}$, $C(O)R^{11}$, $C(S)R^{11}$, CO_2R^{11}, $C(O)SR^{11}$, $C(O)NR^{11}R^{12}$, $C(S)NR^{11}R^{12}$, $C(O)N(OH)R^{12}$, $C(S)N(OH)R^{11}$, $NR^{11}C(O)R^{12}$, $NR^{11}C(S)R^{12}$, $N(OH)C(O)R^{12}$, $N(OH)C(S)R^{11}$, $NR^{11}CO_2R^{12}$, $NR^{11}C(O)NR^{12}R^{13}$, and $NR^{11}C(S)NR^{12}R^{13}$, $N(OH)CO_2R^{11}$, $NR^{11}C(O)SR^{12}$, $N(OH)C(O)NR^{11}R^{12}$, $N(OH)C(S)NR^{11}R^{12}$, $NR^{11}C(O)N(OH)R^{12}$, $NR^{11}C(S)N(OH)R^{12}$, $NR^{11}SO_2R^{12}$, $NHSO_2NR^{11}R^{12}$, $NR^{11}SO_2NHR^{12}$, $P(O)(OR^{11})(OR^{12})$, wherein t is an integer between 1 and 2, R^{11}, R^{12} and R^{13} are each independently selected from the group comprising hydrogen, alkyl, alkenyl, and alkynyl; and

wherein R^5 is selected from the group comprising hydrogen, oxo, hydroxyl, alkyl, alkenyl, alkynyl, alkanediyl, alkyloxy, alkyloxyalkyl, arylcarbonylalkyl, alkylcarbonylalkyl, alkanoyl, cycloalkylcarbonylalkyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkanoyl, aryl, aralkyl, arylalkenyl, arylcarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aryloxyalkyl, haloalkyl, hydroxyalkyl, aralkanoyl, aryloxycarbonylalkyl, aryloxyalkanoyl, Het^1, Het^1alkyl, Het^1oxy, Het^1oxyalkyl, Het^1aryl, Het^1aralkyl, Het^1cycloalkyl, Het^1aryloxyalkyl, Het^1aroyl, Het^2, Het^2oxy, Het^2alkyl; Het^2oxyalkyl, Het^2aralkyl, Het^2cycloalkyl, Het^2aryl, Het^2alkanoyl, Het^2aralkanoyl, Het^2aroyl, Het^2aryloxyalkyl, aminocarbonyl, aminoalkanoyl, aminoalkyl, optionally substituted by one or more substituents independently selected from the group comprising alkyl, aralkyl,

aryl, Het^1, Het^2, cycloalkyl, alkyloxycarbonyl, carboxyl, aminocarbonyl, mono- or di(alkyl)aminocarbonyl, aminosulfonyl, alkyl$S(=O)_t$, hydroxy, cyano, halogen or amino optionally mono- or disubstituted wherein the substituents are independently selected from the group comprising alkyl, aryl, aralkyl, aryloxy, arylamino, arylthio, aryloxyalkyl, arylaminoalkyl, aralkoxy, alkylthio, alkoxy, aryloxyalkoxy, aylaminoalkoxy, aralkylamino, aryloxyalkylamino, arylaminoalkylamino, arylthioalkoxy, arylthioalkylamino, aralkylthio, aryloxyalkylthio, arylaminoalkylthio, arylthioalkylthio, alkylamino, cycloalkyl, cycloalkylalkyl, Het^1, Het^2, Het^1alkyl, Het^2alkyl, Het^1amino, Het^2amino, Het^1alkylamino, Het^2alkylamino, Het^1thio, Het^2thio, Het^1alkylthio, Het^2alkylthio, Het^1oxy and Het^2oxy, OR^{11}, SR^{11}, $SO_2NR^{11}R^{12}$, $SO_2N(OH)R^{11}$, CN, $CR^{11}=NR^{12}$, $S(O)R^{11}$, SO_2R^{11}, $CR^{11}=N(OR^{12})$, N_3, NO_2, $NR^{11}R^{12}$, $N(OH)R^{11}$, $C(O)R^{11}$, $C(S)R^{11}$, CO_2R^{11}, $C(O)SR^{11}$, $C(O)NR^{11}R^{12}$, $C(S)NR^{11}R^{12}$, $C(O)N(OH)R^{12}$, $C(S)N(OH)R^{11}$, $NR^{11}C(O)R^{12}$, $NR^{11}C(S)R^{12}$, $N(OH)C(O)R^{12}$, $N(OH)C(S)R^{11}$, $NR^{11}CO_2R^{12}$, $NR^{11}C(O)NR^{12}R^{13}$, and $NR^{11}C(S)NR^{12}R^{13}$, $N(OH)CO_2R^{11}$, $NR^{11}C(O)SR^{12}$, $N(OH)C(O)NR^{11}R^{12}$, $N(OH)C(S)NR^{11}R^{12}$, $NR^{11}C(O)N(OH)R^{12}$, $NR^{11}C(S)N(OH)R^{12}$, $NR^{11}SO_2R^{12}$, $NHSO_2NR^{11}R^{12}$, $NR^{11}SO_2NHR^{12}$, $P(O)(OR^{11})(OR^{12})$, wherein t is an integer between 1 and 2, R^{11}, R^{12} and R^{13} are each independently selected from the group comprising hydrogen, alkyl, alkenyl, and alkynyl.

2. A compound according to claim 1, having the formula I or a pharmaceutically acceptable salt thereof,

formula I



wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxy, alkyloxyalkyl, alkylthioalkyl, alkyloxycarbonyl, alkylthiocarbonyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylthiocarbonyl, cycloalkylalkoxycarbonyl, cycloalkylalkoxythiocarbonyl, cycloalkylthioalkyl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, cycloalkylcarbonyloxyalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, aryloxycarbonyl, arylthiocarbonyl, aralkoxycarbonyl, arylalkylthiocarbonyl, aryloxyalkyl, arylthioalkyl, haloalkyl,

hydroxyalkyl, aralkanoyl, aroyl, aryloxycarbonylalkyl, aryloxyalkanoyl, carboxyl, formyl, alkenylcarbonyl, alkynylcarbonyl, Het^1, Het^1alkyl, Het^1oxyalkyl, Het^1aryl, Het^1aralkyl, Het^1cycloalkyl, Het^1carbonyl, Het^1alkoxycarbonyl, Het^1alkylthiocarbonyl, Het^1oxycarbonyl, Het^1thiocarbonyl, Het^1alkanoyl, Het^1aralkanoyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^1aryloxycarbonyl, Het^1aralkoxycarbonyl, Het^1aroyl, Het^1oxyalkylcarbonyl, Het^1alkyloxyalkylcarbonyl, Het^1aryloxyalkylcarbonyl, Het^1carbonyloxyalkyl, Het^1alkylcarbonyloxyalkyl, Het^1aralkylcarbonyloxyalkyl, Het^2alkyl; Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aralkyl, Het^2carbonyl, Het^2oxycarbonyl, Het^2thiocarbonyl, Het^2alkanoyl, Het^2alkylthiocarbonyl, Het^2alkoxycarbonyl, Het^2aralkanoyl, Het^2aralkoxycarbonyl, Het^2aryloxycarbonyl, Het^2aroyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, Het^2oxyalkylcarbonyl, Het^2alkyloxyalkylcarbonyl, Het^2aryloxyalkylcarbonyl, Het^2carbonyloxyalkyl, Het^2alkylcarbonyloxyalkyl, Het^2aralkylcarbonyloxyalkyl, cyano, aminocarbonyl, aminoalkanoyl, aminoalkyl, $CR^6=NR^7$ or $CR^6=N(OR^7)$, with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^2 and R^3 are independently selected from the group comprising hydroxyl, alkyloxy, alkylsilyloxy, arylsilyloxy, alkyloxyalkyloxy, cycloalkyloxy cycloalkylalkyloxy, aralkyloxy, aryloxyalkyloxy, silyloxy, alkylcarbonyloxy, arylcarbonyloxy, cycloalkylcarbonyloxy, haloalkyloxy, hydroxyalkyloxy, aralkanoyloxy, aroyloxy, aryloxycarbonylalkyloxy, formyloxy, Het^1alkyloxy, Het^1oxy, Het^1oxyalkyloxy, Het^1aryloxy, Het^1aralkyloxy, Het^1cycloalkyloxy, Het^1carbonyloxy, Het^1oxycarbonyloxy, Het^1alkanoyloxy, Het^1aralkanoyloxy, Het^1aryloxyalkyloxy, Het^1aroyl, Het^2oxy, Het^2alkyloxy; Het^2oxyalkyloxy, Het^2aralkyloxy, Het^2cycloalkyloxy, Het^2alkanoyloxy, Het^2aralkanoyloxy, Het^2carbonyloxyl, Het^2aryloxy, Het^2aryloxyalkyloxy,

wherein R^1 R^2 and R^3 are optionally substituted by one or more substituents independently selected from the group comprising alkyl, aralkyl, aryl, Het^1, Het^2, cycloalkyl, alkyloxycarbonyl, carboxyl, aminocarbonyl, mono- or di(alkyl)aminocarbonyl, aminosulfonyl, $alkylS(=O)_t$, hydroxy, cyano, halogen or amino optionally mono- or disubstituted wherein the substituents are independently selected from the group comprising alkyl, aryl, aralkyl, aryloxy, arylamino, arylthio, aryloxyalkyl, arylaminoalkyl, aralkoxy, alkylthio, alkoxy, aryloxyalkoxy, arylaminoalkoxy, aralkylamino, aryloxyalkylamino, arylaminoalkylamino, arylthioalkoxy, arylthioalkylamino, aralkylthio, aryloxyalkylthio, arylaminoalkylthio, arylthioalkylthio,

alkylamino, cycloalkyl, cycloalkylalkyl, Het^1, Het^2, Het^1alkyl, Het^2alkyl, Het^1amino, Het^2amino, Het^1alkylamino, Het^2alkylamino, Het^1thio, Het^2thio, Het^1alkylthio, Het^2alkylthio, Het^1oxy and Het^2oxy, OR^8, SR^8, $SO_2NR^8R^9$, $SO_2N(OH)R^8$, CN, $CR^8=NR^9$, $S(O)R^8$, SO_2R^8, $CR^8=N(OR^9)$, N_3, NO_2, NR^8R^9, $N(OH)R^8$, $C(O)R^8$, $C(S)R^8$, CO_2R^8, $C(O)SR^8$, $C(O)NR^8R^9$, $C(S)NR^8R^9$, $C(O)N(OH)R^9$, $C(S)N(OH)R^8$, $NR^8C(O)R^9$, $NR^8C(S)R^9$, $N(OH)C(O)R^9$, $N(OH)C(S)R^8$, $NR^8CO_2R^9$, $NR^8C(O)NR^9R^{10}$, and $NR^8C(S)NR^9R^{10}$, $N(OH)CO_2R^8$, $NR^8C(O)SR^9$, $N(OH)C(O)NR^8R^9$, $N(OH)C(S)NR^8R^9$, $NR^8C(O)N(OH)R^9$, $NR^8C(S)N(OH)R^9$, $NR^8SO_2R^9$, $NHSO_2NR^8R^9$, $NR^8SO_2NHR^9$, $P(O)(OR^8)(OR^9)$,

with t being an integer between 1 and 2, and R^8 R^9 and R^{10} being each independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^4 is oxo and R^5 is hydrogen or alkyl.

3. A compound according to claim 1,

wherein R^1 is selected from the group comprising hydrogen, alkyl, hydroxyalkyl, alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, alkyloxycarbonyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylalkoxycarbonyl, cycloalkylthioalkyl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, cycloalkylcarbonyloxyalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, aryloxycarbonyl, aralkoxycarbonyl, arylthioalkyl, aralkanoyl, aroyl, carboxyl, formyl, alkenylcarbonyl, alkynylcarbonyl, Het^1oxyalkyl, Het^1alkoxycarbonyl, Het^1oxycarbonyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^1aryloxycarbonyl, Het^1aralkoxycarbonyl, Het^1oxyalkylcarbonyl, Het^1alkyloxyalkylcarbonyl, Het^1aryloxyalkylcarbonyl, Het^1carbonyloxyalkyl, Het^1alkylcarbonyloxyalkyl, Het^1aralkylcarbonyloxyalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2oxycarbonyl, Het^2alkoxycarbonyl, Het^2aralkoxycarbonyl, Het^2aryloxycarbonyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, Het^2oxyalkylcarbonyl, Het^2alkyloxyalkylcarbonyl, Het^2aryloxyalkylcarbonyl, Het^2carbonyloxyalkyl, Het^2alkylcarbonyloxyalkyl, Het^2aralkylcarbonyloxyalkyl, $CR^6=NR^7$, $CR^6=N(OR^7)$,

with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^2 and R^3 are independently selected from the group comprising hydroxyl, alkyloxy, alkyloxyalkyloxy, cycloalkyloxy cycloalkylalkyloxy, aralkyloxy, aryloxyalkyloxy, silyloxy, alkylcarbonyloxy, arylcarbonyloxy, cycloalkylcarbonyloxy, aryloxycarbonylalkyloxy, formyloxy, Het^1alkyloxy, Het^1oxy, Het^1oxyalkyloxy, Het^1aryloxy, Het^1aralkyloxy, Het^1cycloalkyloxy, Het^1carbonyloxy, Het^1alkanoyloxy, Het^1aralkanoyloxy, Het^1aryloxyalkyloxy, Het^2oxy, Het^2alkyloxy; Het^2oxyalkyloxy, Het^2aralkyloxy, Het^2cycloalkyloxy, Het^2alkanoyloxy, Het^2aralkanoyloxy, Het^2carbonyloxyl, Het^2aryloxy, Het^2aryloxyalkyloxy,

wherein R^1 R^2 and R^3 are optionally substituted by one or more substituents independently selected from the group indicated in claim 1; and

wherein R^4 is selected from the group comprising, oxo, hydroxyalkyl, alkyl, alkenyl, alkylcarbonylalkyl, arylcarbonylalkyl and R^5 is hydrogen, oxo, hydroxyl, hydroxyalkyl, alkyl, alkenyl, alkylcarbonylalkyl, arylcarbonylalkyl.

4. A compound according to claim 1 or 2,

wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, alkyloxycarbonyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylalkoxycarbonyl, cycloalkylthioalkyl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, cycloalkylcarbonyloxyalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, aryloxycarbonyl, aralkoxycarbonyl, arylthioalkyl, aralkanoyl, aroyl, carboxyl, formyl, alkenylcarbonyl, alkynylcarbonyl, Het^1oxyalkyl, Het^1alkoxycarbonyl, Het^1oxycarbonyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^1aryloxycarbonyl, Het^1aralkoxycarbonyl, Het^1oxyalkylcarbonyl, Het^1alkyloxyalkylcarbonyl, Het^1aryloxyalkylcarbonyl, Het^1carbonyloxyalkyl, Het^1alkylcarbonyloxyalkyl, Het^1aralkylcarbonyloxyalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2oxycarbonyl, Het^2alkoxycarbonyl, Het^2aralkoxycarbonyl, Het^2aryloxycarbonyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, Het^2oxyalkylcarbonyl, Het^2alkyloxyalkylcarbonyl, Het^2aryloxyalkylcarbonyl, Het^2carbonyloxyalkyl, Het^2alkylcarbonyloxyalkyl, Het^2aralkylcarbonyloxyalkyl, $CR^6=NR^7$, $CR^6=N(OR^7)$,

with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^2 and R^3 are independently selected from the group comprising hydroxyl, alkyloxy, alkyloxyalkyloxy, cycloalkyloxy cycloalkylalkyloxy, aralkyloxy, aryloxyalkyloxy,

silyloxy, alkylcarbonyloxy, arylcarbonyloxy, cycloalkylcarbonyloxy, aryloxycarbonylalkyloxy, formyloxy, Het^{1}alkyloxy, Het^{1}oxy, Het^{1}oxyalkyloxy, Het^{1}aryloxy, Het^{1}aralkyloxy, Het^{1}cycloalkyloxy, Het^{1}carbonyloxy, Het^{1}alkanoyloxy, Het^{1}aralkanoyloxy, Het^{1}aryloxyalkyloxy, Het^{2}oxy, Het^{2}alkyloxy; Het^{2}oxyalkyloxy, Het^{2}aralkyloxy, Het^{2}cycloalkyloxy, Het^{2}alkanoyloxy, Het^{2}aralkanoyloxy, Het^{2}carbonyloxyl, Het^{2}aryloxy, Het^{2}aryloxyalkyloxy,

wherein R^1 R^2 and R^3 are optionally substituted by one or more substituents independently selected from the group indicated in claim 1; and

wherein R^4 is oxo and R^5 is hydrogen or alkyl.

5. A compound according to claim 1, 2 or 4,

wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylthioalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, arylthioalkyl, aralkanoyl, aroyl, carboxyl, formyl, alkenylcarbonyl, alkynylcarbonyl, Het^{1}oxyalkyl, Het^{1}aryloxyalkyl, Het^{1}alkyloxyalkyl, Het^{1}arylthioalkyl, Het^{1}oxyalkylcarbonyl, Het^{1}alkyloxyalkylcarbonyl, Het^{1}aryloxyalkylcarbonyl, Het^{2}oxyalkyl, Het^{2}alkyloxyalkyl, Het^{2}aryloxyalkyl, Het^{2}arylthioalkyl, Het^{2}oxyalkylcarbonyl, Het^{2}alkyloxyalkylcarbonyl, Het^{2}aryloxyalkylcarbonyl, $CR^6{=}NR^7$, $CR^6{=}N(OR^7)$,

with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^{1}alkyl, Het^{1}aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^2 and R^3 are independently selected from the group comprising hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, cycloalkylcarbonyloxy, formyloxy, Het^{1}carbonyloxy, Het^{1}alkanoyloxy, Het^{1}aralkanoyloxy, Het^{2}carbonyloxyl, Het^{2}alkanoyloxy, Het^{2}aralkanoyloxy,

wherein R^1 R^2 and R^3 are optionally substituted by one or more substituents independently selected from the group indicated in claim 1; and

wherein R^4 is oxo and R^5 is hydrogen or alkyl.

6. A compound according to any of claims 1, 2, 4 to 5, wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, cycloalkylalkyl, cycloalkylthioalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylthioalkyl, carboxyl, formyl, Het^{1}oxyalkyl, Het^{1}aryloxyalkyl, Het^{1}alkyloxyalkyl, Het^{1}arylthioalkyl, Het^{2}oxyalkyl, Het^{2}alkyloxyalkyl, Het^{2}aryloxyalkyl, Het^{2}arylthioalkyl, optionally substituted by one or more

substituents independently selected from the group indicated in claim 1; wherein R^2 and R^3 are hydroxyl and wherein R^4 is oxo and R^5 is hydrogen.

7. A compound according to any of claims 1, 2, 4 to 6, wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, cycloalkylalkyl, silyloxyalkyl, aralkyl, arylalkenyl, carboxyl, formyl, Het^1oxyalkyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aryloxyalkyl, optionally substituted by one or more substituents independently selected from the group indicated in claim 1; wherein R^2 and R^3 are hydroxyl, R^4 is oxo and R^5 is hydrogen.

8. A compound according to any of claims 1, 2, 4 to 7, wherein R^1 is selected from the group comprising alkyl, carboxyl, formyl; wherein R^2 and R^3 are hydroxyl, and wherein R^4 is oxo and R^5 is hydrogen.

9. A compound according to claim 8, wherein R^1 is formyl, R^2 and R^3 are hydroxyl R^4 is oxo and R^5 is hydrogen.

10. A compound according to claim 1 or 3,

wherein R^1 is selected from the group comprising hydrogen, alkyl, alkenyl, alkynyl, alkyloxyalkyl, hydroxyalkyl, alkylthioalkyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylthioalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, arylthioalkyl, aralkanoyl, aroyl, carboxyl, formyl, alkenylcarbonyl, alkynylcarbonyl, Het^1oxyalkyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^1oxyalkylcarbonyl, Het^1alkyloxyalkylcarbonyl, Het^1aryloxyalkylcarbonyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, Het^2oxyalkylcarbonyl, Het^2alkyloxyalkylcarbonyl, Het^2aryloxyalkylcarbonyl, $CR^6{=}NR^7$, $CR^6{=}N(OR^7)$,

with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^2 and R^3 are independently selected from the group comprising hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, cycloalkylcarbonyloxy, formyloxy, Het^1carbonyloxy, Het^1alkanoyloxy, Het^1aralkanoyloxy, Het^2carbonyloxyl, Het^2alkanoyloxy, Het^2aralkanoyloxy,

wherein R^1 R^2 and R^3 are optionally substituted by one or more substituents independently selected from the group indicated in claim 1; and

wherein R^4 is oxo, hydroxyalkyl, alkyl, alkenyl, arylcarbonylaryl, alkylcarbonylalkyl and R^5 is hydrogen or alkyl.

11. A compound according to any of claims 1, 3 or 10, wherein R^1 is hydroxyalkyl, R^2 and R^3 are hydroxyl, R^4 is oxo and R^5 is hydrogen.

12. A compound according to any of claims 1, 3 or 10, wherein R^1 is selected from the group comprising hydrogen, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkyloxyalkyl, alkylthioalkyl, cycloalkylalkyl, cycloalkylthioalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylthioalkyl, carboxyl, formyl, Het^1oxyalkyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, optionally substituted by one or more substituents independently selected from the group indicated in claim 1; wherein R^2 and R^3 are hydroxyl and wherein R^4 is hydroxyalkyl, arylcarbonylalkyl, alkylcarbonylalkyl and R^5 is hydrogen.

13. A compound according to any of claims 1, 3, 10 or 12, wherein R^1 is selected from the group comprising hydrogen, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkyloxyalkyl, cycloalkylalkyl, silyloxyalkyl, aralkyl, arylalkenyl, carboxyl, formyl, Het^1oxyalkyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aryloxyalkyl, optionally substituted by one or more substituents independently selected from the group indicated in claim 1; wherein R^2 and R^3 are hydroxyl, R^4 is hydroxyalkyl, arylcarbonylalkyl, alkylcarbonylalkyl and R^5 is hydrogen.

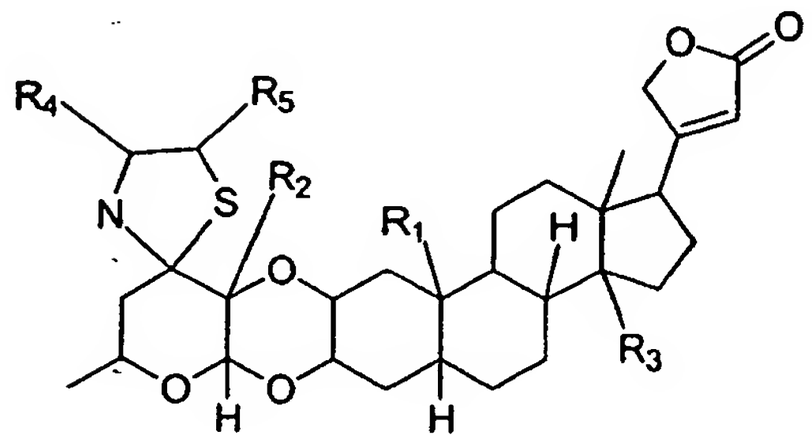
14. A compound according to any of claims 1, 3, 10, 12 or 13, wherein R^1 is selected from the group comprising alkyl, hydroxyalkyl, carboxyl, formyl; wherein R^2 and R^3 are hydroxyl, and wherein R^4 is arylcarbonylalkyl and R^5 is hydrogen.

15. A compound according to claim 14, wherein R^1 is hydroxyalkyl, R^2 and R^3 are hydroxyl, R^4 is arylcarbonylalkyl and R^5 is hydrogen.

16. A compound according to claim 15, wherein R^1 is hydroxymethylene, R^2 and R^3 are hydroxyl, R^4 is phenylcarbonylmethylene and R^5 is hydrogen.

17. A compound having the formula Ia or a pharmaceutically acceptable salt or ester thereof,

formula Ia



wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, alkyloxycarbonyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylalkoxycarbonyl, cycloalkylthioalkyl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, cycloalkylcarbonyloxyalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, aryloxycarbonyl, aralkoxycarbonyl, arylthioalkyl, aralkanoyl, aroyl, silyloxyalkyl, carboxyl, alkenylcarbonyl, alkynylcarbonyl, Het^1oxyalkyl, Het^1alkoxycarbonyl, Het^1oxycarbonyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^1aryloxycarbonyl, Het^1aralkoxycarbonyl, Het^1oxyalkylcarbonyl, Het^1alkyloxyalkylcarbonyl, Het^1aryloxyalkylcarbonyl, Het^1carbonyloxyalkyl, Het^1alkylcarbonyloxyalkyl, Het^1aralkylcarbonyloxyalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2oxycarbonyl, Het^2alkoxycarbonyl, Het^2aralkoxycarbonyl, Het^2aryloxycarbonyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, Het^2oxyalkylcarbonyl, Het^2alkyloxyalkylcarbonyl, Het^2aryloxyalkylcarbonyl, Het^2carbonyloxyalkyl, Het^2alkylcarbonyloxyalkyl, Het^2aralkylcarbonyloxyalkyl,$CR^6=NR^7$, $CR^6=N(OR^7)$,

with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^2 and R^3 have the same definition as in claim 1;

wherein R^1 R^2 and R^3 are optionally substituted by one or more substituents independently selected from the group as indicated in claim 1, and

wherein R^4 and R^5 are hydrogen or alkyl.

18. A compound according to claim 17,

wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylthioalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, arylthioalkyl, aralkanoyl, aroyl, silyloxyalkyl, carboxyl, alkenylcarbonyl, alkynylcarbonyl, Het^1oxyalkyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^1oxyalkylcarbonyl, Het^1alkyloxyalkylcarbonyl, Het^1aryloxyalkylcarbonyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, Het^2oxyalkylcarbonyl, Het^2alkyloxyalkylcarbonyl, Het^2aryloxyalkylcarbonyl, $CR^6=NR^7$, $CR^6=N(OR^7)$, with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^2 and R^3 have the same definition as in claim 1;

wherein R^1 R^2 and R^3 are optionally substituted by one or more substituents independently selected from the group as indicated in claims 1, and

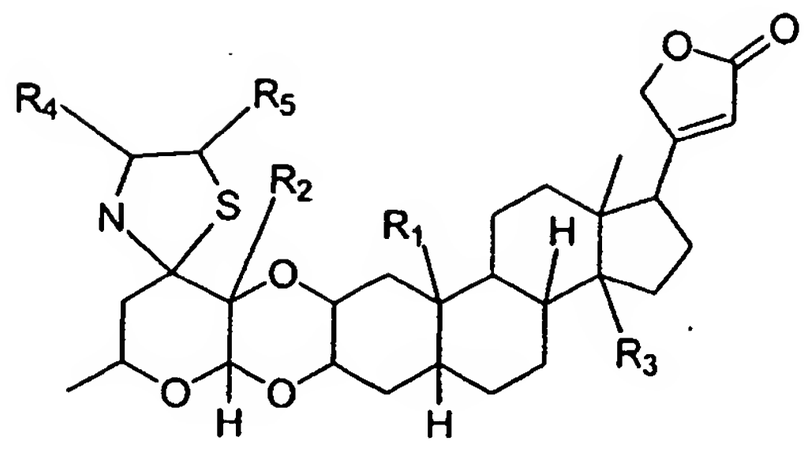
wherein R^4 and R^5 are hydrogen or alkyl.

19. A compound according to claim 17 or 18, wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, cycloalkylalkyl, cycloalkylthioalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylthioalkyl, silyloxyalkyl, carboxyl, Het^1oxyalkyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, optionally substituted by one or more substituents independently selected from the group indicated in claim 1; wherein R^2 and R^3 are hydroxyl and wherein R^4 and R^5 are hydrogen or alkyl.

20. A compound according to any of claims 17 to 19, wherein R^1 is selected from the group comprising alkyl, alkenyl, alkynyl, alkyloxyalkyl, cycloalkylalkyl, silyloxyalkyl, aralkyl, arylalkenyl, carboxyl, Het^1oxyalkyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2aryloxyalkyl, optionally substituted by one or more substituents independently selected from the group indicated in claim 1; wherein R^2 and R^3 are hydroxyl and wherein R^4 and R^5 are hydrogen.

21. A compound having the formula Ib or a pharmaceutically acceptable salt or ester thereof,

formula Ib



wherein R^1 is selected from the group comprising alkenyl, alkynyl, alkyloxyalkyl, alkylthioalkyl, alkyloxycarbonyl, alkanoyl, cycloalkylalkyl, cycloalkylcarbonyl, cycloalkylalkanoyl, cycloalkylalkoxycarbonyl, cycloalkylthioalkyl, alkylcarbonyloxyalkyl, arylcarbonyloxyalkyl, cycloalkylcarbonyloxyalkyl, silyloxyalkyl, aralkyl, arylalkenyl, arylcarbonyl, aryloxycarbonyl, aralkoxycarbonyl, arylthioalkyl, aralkanoyl, aroyl, silyloxyalkyl, carboxyl, alkenylcarbonyl, alkynylcarbonyl, Het^1oxyalkyl, Het^1alkoxycarbonyl, Het^1oxycarbonyl, Het^1aryloxyalkyl, Het^1alkyloxyalkyl, Het^1arylthioalkyl, Het^1aryloxycarbonyl, Het^1aralkoxycarbonyl, Het^1oxyalkylcarbonyl, Het^1alkyloxyalkylcarbonyl, Het^1aryloxyalkylcarbonyl, Het^1carbonyloxyalkyl, Het^1alkylcarbonyloxyalkyl, Het^1aralkylcarbonyloxyalkyl, Het^2oxyalkyl, Het^2alkyloxyalkyl, Het^2oxycarbonyl, Het^2alkoxycarbonyl, Het^2aralkoxycarbonyl, Het^2aryloxycarbonyl, Het^2aryloxyalkyl, Het^2arylthioalkyl, Het^2oxyalkylcarbonyl, Het^2alkyloxyalkylcarbonyl, Het^2aryloxyalkylcarbonyl, Het^2carbonyloxyalkyl, Het^2alkylcarbonyloxyalkyl, Het^2aralkylcarbonyloxyalkyl,$CR^6=NR^7$, $CR^6=N(OR^7)$,

with R^6 and R^7 being independently selected from the group comprising hydrogen, hydroxyl, alkyl, aryl, Het^1, Het^1alkyl, Het^1aryl, alkenyl, alkynyl, aminoalkyl, aminoaryl, alkylcarbonylamino, arylcarbonylamino, alkylthiocarbonylamino and arylthiocarbonylamino;

wherein R^1 is optionally substituted by one or more substituents independently selected from the group as indicated in claim 1, and

wherein R^2 and R^3 are hydroxyl and wherein R^4 is replaced by a double bond between the N atom and the C carbon atom of the N-containing heterocyclic ring of formula I; and wherein R^5 is hydrogen.

22. A compound according to claim 21, wherein R^1 is selected from the group comprising alkenyl, alkynyl, alkyloxyalkyl, cycloalkylalkyl, silyloxyalkyl, aralkyl, arylalkenyl, carboxyl,

Het^{1}oxyalkyl, Het^{1}aryloxyalkyl, Het^{1}alkyloxyalkyl, Het^{2}oxyalkyl, Het^{2}alkyloxyalkyl, Het^{2}aryloxyalkyl, optionally substituted by one or more substituents independently selected from the group indicated in claim 1; wherein R^2 and R^3 are hydroxyl and wherein R^4 and R^5 are hydrogen.

23. A compound according to claim 22, wherein R^1 has the same definition as in claim 20, wherein R^2 and R^3 are hydroxyl; wherein R^4 is replaced by a double bond between the N atom and the C carbon atom of the N-containing heterocyclic ring of formula I; and wherein R^5 is hydrogen.

24. Compound of formula I, wherein R^1 is hydroxyalkyl, wherein R^2 and R^3 are hydroxyl; wherein R^4 is replaced by a double bond between the N atom and the C carbon atom of the N-containing heterocyclic ring of formula I; and wherein R^5 is hydrogen.

25. Compound of formula I or a pharmaceutically acceptable salt or ester thereof, wherein R^1, R^2, R^3, R^4 and R^5 are selected as in Table A.

26. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound according to any of claims 1-25.

27. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound according to claim 9.

28. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a therapeutically effective amount of a compound according to claim 11.

29. A compound according to any of claims 1 to 25 for use as a medicament.

30. Use of a compound according to any of claims 1 to 25 for the preparation of a medicament for treating cancer.

31. Use of a compound according to any of claims 1 to 25 in the treatment of cancer.

32. Method of treating cancer comprising administrating to an individual in need of such treatment a pharmaceutical composition according to any of claims 26 to 28.